Claims

1. A method of identifying chemical substances which have potential pharmacological activity using nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers of nematode worms into each of the wells of a multi-well assay plate;

(b) contacting the nematode worms with a chemical substance;

(c) detecting a signal indicating phenotypic, physiological, behavioural or biochemical changes in the nematode worms using non-visual detection means.

2. A method of determining the mode of action of a chemical substance using nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers of a panel of different mutant nematode worms into each of the wells of a multi-well assay plate;

(b) contacting the nematode worms with the chemical substance; and

(c) detecting a signal indicating phenotypic, physiological, behavioural or biochemical changes in the nematode worms using non-visual detection means.

3. A method of identifying further components of the biochemical pathway on which a compound having a defined effect on a nematode worm acts, which method comprises the steps of:

(a) subjecting a population of nematode worms to random mutagenesis;

(b) dispensing one mutagenized F1 nematode worm into each of the wells of a multi-well assay plate;

(c) allowing the F1 nematode worms to generate F2 offspring;

(d) contacting the nematode worms with the compound; and

(e) detecting a signal indicating phenotypic, physiological, behavioural or biochemical changes in the nematode worms using non-visual detection means.

4. A method as claimed in claim 3 which further comprises steps of isolating a gene which is mutated in nematode worms which generate a signal in part (e) using genetic techniques.

5. A method of identifying chemical substances which modulate the effect of a first compound, which compound has a defined effect on nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers nematode worms into each of the wells of a multi-well assay plate;

(b) contacting the nematode worms with the first compound;

(c) contacting the nematode worms with a further chemical substance; and

(d) detecting a signal indicating phenotypic, physiological, behavioural or biochemical changes in the nematode worms using non-visual detection means.

6. A method as claimed in claim 5 wherein the second chemical substance suppresses the defined effect of the first compound on the nematode worms.

7. A method as claimed in claim 5 wherein the second chemical substance enhances the defined effect of the first compound on the nematode worms.

8. A method as claimed in any one of claims 1 to 7 wherein the nematode worms are worms are microscopic nematodes.

9. A method as claimed in claim 8 wherein the nematode worms are *C. elegans* or *C. briggsae.*

10. A method as claimed in any one of the preceding claims wherein the step of detecting a signal comprises detecting a change in a measurable property of a marker molecule, whereby a change in the property of the marker molecule indicates a phenotypic, physiological, behavioural or biochemical change in the nematode worms.

11. A method as claimed in claim 10 wherein the marker molecule is a fluorescent molecule, a luminescent molecule or a coloured molecule.

12. A method as claimed in claim 10 wherein the marker molecule is a precursor of a fluorescent molecule, a precursor of a luminescent molecule or a precursor of a coloured molecule.

13. A method as claimed in claim 12 wherein said marker molecule is capable of being cleaved by the action of an enzyme present in the gut of *C. elegans* to generate a fluorescent molecule, a luminescent molecule or a coloured molecule.

14. A method as claimed in claim 10 wherein the marker molecule is a genetically encoded marker molecule.

15. A method as claimed in claim 14 wherein the nematodes are transgenic nematodes which express the genetically encoded marker molecule.

16. A method as claimed in claim 14 or claim 15 wherein the genetically encoded marker molecule is an autonomous fluorescent protein, alkaline phosphatase, luciferase, β-glucuronidase, β-lactamase, β-galactosidase, acetohydroxyacid synthase, chloramphenicol acetyl transferase, horseradish peroxidase, nopaline synthase, octapine synthase or aequorin.

17. A method as claimed in any one of claims 1 to 16 wherein the non-visual detection means is a multi-well plate reader.

18. A method as claimed in claim 17 wherein the multi-well plate reader performs luminescence, fluorescence or spectrophotometric detection.

19. A method as claimed in any one of claims 1 to 16 wherein the non-visual detection means is a FANS device.

20. A method as claimed in claim 19 wherein the FANS device performs luminescence, fluorescence or spectrophotometric detection.

21. A method as claimed in any one of claims 1 to 9 wherein the step of detecting a signal comprises detecting the size and/or developmental stage of the nematode worms using a FANS device.

22. A method as claimed in claim 21 which comprises detecting eggs, L1 stage, L2 stage, L3 stage, L4 stage, adult worms or dauer worms.

23. A method as claimed in any one of the preceding claims wherein step (a) comprises dispensing substantially equal volumes of a homogeneous suspension of nematode worms into each of the wells of the multi-well assay plate.

24. A method as claimed in claim 23 wherein the homogeneous suspension comprises a suspension of *C. elegans* in a viscous solution.

25. A method as claimed in claim 24 wherein the viscous solution comprises a solution of a polymer material.

26. A method as claimed in claim 25 wherein the polymer material is low melting point agarose.

27. A method as claimed in any one of the preceding claims wherein the nematode worms are synchronized in the same growth stage.

28. A method as claimed in claim 27 wherein the nematode worms are eggs, L1 stage, L2 stage, L3 stage, L4 stage, adult worms or dauer worms.

29. A method as claimed in claim 27 or claim 28 wherein the worms are hermaphrodites or males.

30. A method as claimed in any one of the preceding claims wherein the nematode worms are a wild type strain, a mutant strain, a transgenic strain or a humanized strain.

31. A method as claimed in claim 30 wherein said nematode worms are a humanized strain expressing one or more protein-encoding nucleic acid sequences of human origin.

32. A method as claimed in claim 30 wherein said nematode worms are transgenic *C. elegans* expressing a transgene comprising a toxic gene.

33. A method as claimed in claim 32 wherein said toxic gene encodes ataxin, alpha-synuclein, ubiquitin, the tau gene product, the Huntington's gene product, the best macular dystrophy gene product, the age-related macular dystrophy product or the unc-53 gene product.

34. A method as claimed in claimed in claim 32 or claim 33 wherein expression of the toxic gene is driven by a tissue-specific promoter which is capable of directing gene expression in a single tissue, a sub-set of cell types, a single cell type or a single cell of *C. elegans*.

35. A method as claimed in claim 34 wherein expression of the toxic gene is driven by the daf-7 promoter.

36. A method as claimed in any one of the preceding claims wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to increase the viscosity of the medium.

37. A method as claimed in claim 36 wherein the water soluble polymer is carboxymethyl cellulose, low melting point agarose or polyethylene glycol.

38. A method as claimed in claim 37 wherein the water soluble polymer is medium viscosity carboxymethyl cellulose.

39. A method as claimed in any one of claims 36 to 39 wherein the concentration of water soluble polymer in the liquid medium is 0.3%.

40. A method as claimed in any one of claims 1 to 35 wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to prevent the nematode worms from sticking to the wells of the multi-well plate.

41. A method as claimed in claim 41 wherein the water soluble polymer is polyethylene glycol, polyvinyl alcohol or polyvinylpyrrolidone.

42. A method as claimed in claim 40 or claim 41 wherein the concentration of water soluble polymer in the liquid medium is from 0.01% to 10%.

43. A method as claimed in claim 42 wherein the concentration of water soluble polymer in the liquid medium is 0.1%.

44. A method of identifying chemical substances which have potential pharmacological activity using nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers of nematode worms into each of the wells of a multi-well assay plate;

(b) contacting the nematode worms with a sample of a chemical substance;

(c) detecting changes in the pharynx pumping rate of the nematode worms using non-visual detection means.

45. A method of determining the mode of action of a chemical substance using nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers of a panel of different mutant, transgenic or humanized nematode worms into each of the wells of a multi-well assay plate;

(b) contacting the nematode worms with the chemical substance; and

(c) detecting changes in the pharynx pumping rate of the nematode worms using non-visual detection means.

46. A method of identifying further components of the biochemical pathway on which a compound having a defined effect on nematode worms acts, which method comprises the steps of:

(a) subjecting a population of nematode worms to random mutagenesis;

(b) dispensing one mutagenized F1 nematode worm into each of the wells of a multi-well assay plate;

(c) allowing the F1 nematode worm to generate F2 offspring;

(d) contacting the nematode worms with the compound; and

(e) detecting changes in the pharynx pumping rate of the nematode worms using non-visual detection means.

47. A method as claimed in claim 46 which further comprises steps of isolating a gene which is mutated in nematode worms which exhibit changes in the pharynx pumping rate in part (e) using genetic techniques.

48. A method of identifying chemical substances which modulate the effect of a first compound, which compound has a defined effect on nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers of nematode worms into each of the wells of a multi-well assay plate;

(b) contacting the nematode worms with the first compound;

(c) contacting the nematode worms with a further chemical substance; and

(d) detecting changes in the pharynx pumping rate of the nematode worms using non-visual detection means.

49. A method as claimed in claim 48 wherein the second chemical substance suppresses the defined effect of the first compound on the nematode worms.

50. A method as claimed in claim 48 wherein the second chemical substance enhances the defined effect of the first compound on the nematode worms.

51. A method as claimed in any one of claims 44 to 50 wherein the nematode worms are microscopic nematodes.

52. A method as claimed in claim 51 wherein the nematode worms are *C. elegans* or *C. briggsae*.

53. A method as claimed in any one of claims 44 to 52 wherein the step of detecting changes in the pharynx pumping rate comprises contacting the nematode worms with a marker molecule which generates a signal when taken up by nematode worms and detecting the said signal using non-visual detection means.

54. A method as claimed in claim 53 wherein the marker molecule is a fluorescent molecule, a luminescent molecule, a coloured molecule, a precursor of a fluorescent marker molecule, a precursor of a luminescent marker molecule or a precursor of a coloured marker molecule.

55. A method as claimed in claim 54 wherein said marker molecule is capable of being cleaved by the action of an enzyme present in the gut of the nematode worms to generate a fluorescent molecule, a luminescent molecule or a coloured molecule.

56. A method as claimed in claim 55 wherein the marker molecule is calcein-AM, BCECF-AM, fluorescein diphosphate (FDP), fluorescein diacetate (FDA), CMB-leu, AMPPD or X-gluc.

57. A method as claimed in claim 55 wherein the marker molecule is sensitive to changes in pH.

58. A method as claimed in any one of claims 44 to 57 wherein the non-visual detection means is a multi-well plate reader.

59. A method as claimed in claim 58 wherein the multi-well plate reader performs luminescence, fluorescence or spectrophotometric detection.

60. A method as claimed in any one of claims 44 to 57 wherein the non-visual detection means is a FANS device.

61. A method as claimed in claim 60 wherein the FANS device performs luminescence, fluorescence or spectrophotometric detection.

62. A method as claimed in any one of claims 44 to 61 wherein said nematode worms are wild-type mutant, transgenic or humanized *C. elegans.*

63. A method as claimed in claim 62 wherein said *C. elegans* exhibit an altered pharynx pumping rate.

64. A method as claimed in claim 62 wherein said mutant *C. elegans* carry a mutation in a gene encoding SERCA protein and/or a PLB protein and/or an SLN protein.

65. A method as claimed in claim 63 wherein said transgenic *C. elegans* express a transgene encoding a SERCA protein or a PLB protein.

66. A method as claimed in claim 65 wherein expression of said transgene is driven by a tissue-specific promoter.

67. A method as claimed in claim 65 or claim 66 wherein the transgenic *C. elegans* further carry a mutation in the *C. elegans* gene encoding SERCA protein.

68. A method as claimed in claim 62 wherein said *C. elegans* exhibit altered levels of one or more of the following neurotransmitters: acetylcholine, serotonin, glutamate, octopamine, GABA or dopamine.

69. A method as claimed in claim 62 wherein said transgenic *C. elegans* expresses a transgene comprising a toxic gene.

70. A method as claimed in claim 69 wherein said toxic gene encodes ataxin, alpha-synuclein, ubiquitin, the tau gene product, the Huntington's gene product, the best

macular dystrophy gene product, the age-related macular dystrophy product or the unc-53 gene product.

71. A method as claimed in claimed in claim 69 or claim 70 wherein expression of the toxic gene is driven by a tissue-specific promoter which is capable of directing gene expression in the *C. elegans* pharynx, in a sub-set of cells of the *C. elegans* pharynx, in the pharyngeal neurons or in a single pharyngeal neuron.

72. A method as claimed in claim 71 wherein expression of the toxic gene is driven by the myo-2 promoter, the unc-129 promoter, the tmy-1 promoter or the daf-7 promoter.

73. A method as claimed in claim 69 or claim 70 wherein expression of the transgene is driven by the daf-7 promoter.

74. A method as claimed in any one of claims 44 to 73 wherein the nematode worms are synchronized in the same growth stage.

75. A method as claimed in claim 74 wherein the nematode worms are eggs, L1 stage, L2 stage, L3 stage, L4 stage, adult worms or dauer worms.

76. A method as claimed in claim 74 or claim 75 wherein the worms are hermaphrodites or males.

77. A method as claimed in any one of claims 44 to 76 wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to increase the viscosity of the medium.

78. A method as claimed in claim 77 wherein the water soluble polymer is carboxymethyl cellulose, low melting point agarose or polyethylene glycol.

79. A method as claimed in claim 78 wherein the water soluble polymer is medium viscosity carboxymethyl cellulose.

80. A method as claimed in any one of claims 77 to 79 wherein the concentration of water soluble polymer in the liquid medium is 0.3%.

81. A method as claimed in any one of claims 44 to 76 wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to prevent the nematode worms from sticking to the wells of the multi-well plate.

82. A method as claimed in claim 81 wherein the water soluble polymer is polyethylene glycol, polyvinyl alcohol or polyvinylpyrrolidone.

83. A method as claimed in claim 81 or claim 82 wherein the concentration of water soluble polymer in the liquid medium is from 0.01% to 10%.

84. A method as claimed in claim 83 wherein the concentration of water soluble polymer in the liquid medium is 0.1%.

85. A method as claimed in claim 44 for use in identifying chemical substances having potential insecticidal activity.

86. A method of identifying chemical substances which have potential pharmacological activity using nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers of nematode worms into each of the wells of a multi-well assay plate;

(b) contacting the nematode worms with a sample of a chemical substance;

(c) detecting changes in the intracellular levels of ions, metabolites or secondary messengers in cells of the nematode worms using non-visual detection means.

87. A method as claimed in claim 86 which comprises detecting changes in the intracellular levels of calcium, cAMP, diacylglycerol or IP3.

88. A method as claimed in claim 87 wherein the nematode worms are transgenic *C. elegans* expressing a genetically encoded marker molecule, which marker molecule generates a signal in response to changes in intracellular levels of ions, metabolites or secondary messengers and step (c) comprises detecting changes in the signal generated by the genetically encoded marker molecule.

89. A method as claimed in claim 88 wherein the genetically encoded marker molecule is GFP-calmodulin or aequorin.

90. A method as claimed in claim 88 or claim 89 wherein the genetically encoded marker molecule is expressed in cells of the pharynx, vulva muscles, body wall muscles or neurons of the transgenic *C. elegans*.

91. A method as claimed in any one of claims 86 to 90 wherein the non-visual detection means is a multi-well plate reader.

92. A method as claimed in claim 91 wherein the multi-well plate reader performs fluorescent, luminescent or spectrophotometric detection.

93. A method as claimed in any one of claims 86 to 90 wherein the non-visual detection means is a FANS device.

94 A method as claimed in claim 93 wherein the FANS device performs fluorescent, luminescent or spectrophotometric detection.

95. A method as claimed in any one of claims 86 to 94 wherein the nematodes are synchronised in the same growth stage.

96. A method as claimed in claim 95 wherein the nematodes are eggs. L1 stage, L2 stage, L3 stage, L4 stage, adult worms or dauer worms.

97. A method as claimed in claim 95 or claim 96 wherein the nematodes are hermaphrodites or males.

98. A method of identifying chemical substances which have potential pharmacological activity using nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers of nematode worms into each of the wells of a multi-well assay plate;

(b) contacting the nematode worms with a sample of a chemical substance;

(c) detecting changes in the movement behaviour of the nematode worms using non-visual detection means.

99. A method of determining the mode of action of a chemical substance using nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers of a panel of different mutant, transgenic or humanized nematode worms into each of the wells of a multi-well assay plate;

(b) contacting the nematode worms with the chemical substance; and

(c) detecting changes in the movement behaviour of the nematode worms using non-visual detection means.

100. A method of identifying further components of the biochemical pathway on which a compound having a defined effect on nematode worms acts, which method comprises the steps of:

(a) subjecting a population of nematode worms to random mutagenesis;

(b) dispensing one mutagenized F1 nematode worm into each of the wells of a multi-well assay plate;

(c) allowing the F1 nematode worms to generate F2 offspring;

(d) contacting the nematode worms with the compound; and

(e) detecting changes in the movement behaviour of the nematode worms using non-visual detection means.

101. A method as claimed in claim 82 which further comprises steps of isolating a gene which is mutated in nematode worms which exhibit a change in movement behaviour in part (e) using genetic techniques.

102. A method of identifying chemical substances which modulate the effect of a first compound, which compound has a defined effect on nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers of nematode worms into each of the wells of a multi-well assay plate;

(b) contacting the nematode worms with the first compound;

(c) contacting the nematode worms with a further chemical substance; and

(d) detecting changes in the movement behaviour of the nematode worms using non-visual detection means.

103. A method as claimed in claim 102 wherein the second chemical substance suppresses the defined effect of the first compound on the nematode worms.

104. A method as claimed in claim 103 wherein the second chemical substance enhances the defined effect of the first compound on the nematode worms.

105. A method as claimed in any one of claims 98 to 104 wherein the nematode worms are microscopic nematodes.

106. A method as claimed in claim 105 wherein the nematode worms are *C. elegans* or *C. briggsae*.

107. A method as claimed in any one of claims 98 to 106 wherein the step of detecting changes in the movement behaviour of the nematode worms comprises

measuring the level of autofluorescence a sub-region of the material in the wells of the multi-well assay plate.

108. A method as claimed in any one of claims 98 to 107 wherein the non-visual detection means is a multi-well plate reader.

109. A method as claimed in claim 98 wherein the multi-well plate reader performs luminescence, fluorescence or spectrophotometric detection.

110. A method as claimed in any one of claims 98 to 109 wherein the nematode worms are synchronized in the same growth stage.

111. A method as claimed in claim 110 wherein the nematode worms are eggs, L1 stage, L2 stage, L3 stage, L4 stage, adult worms or dauer worms.

112. A method as claimed in claim 110 or claim 111 wherein the worms are hermaphrodites or males.

113. A method as claimed in any one of claims 98 to 112 wherein the nematode worms are a wild type strain, a mutant strain, a transgenic strain or a humanized strain.

114. A method as claimed in claim 113 wherein said nematode worms are a humanized strain expressing one or more protein-encoding nucleic acid sequences of human origin.

115. A method as claimed in claim 114 wherein said nematode worms are transgenic *C. elegans* expressing a transgene comprising a toxic gene.

116. A method as claimed in claim 115 wherein said toxic gene encodes ataxin, alpha-synuclein, ubiquitin, the tau gene product, the Huntington's gene product, the best macular dystrophy gene product, the age-related macular dystrophy product or the unc-53 gene product.

117. A method as claimed in claimed in claim 115 or claim 116 wherein expression of the toxic gene is driven by a tissue-specific promoter which is capable of directing gene expression in a single tissue, a sub-set of cell types, a single cell type or a single cell of *C. elegans*.

118. A method as claimed in claim 117 wherein expression of the toxic gene is driven by the daf-7 promoter.

119. A method as claimed in any one of claims 98 to 118 wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to increase the viscosity of the medium.

120. A method as claimed in claim 119 wherein the water soluble polymer is carboxymethyl cellulose, low melting point agarose or polyethylene glycol.

121. A method as claimed in claim 120 wherein the water soluble polymer is medium viscosity carboxymethyl cellulose.

122. A method as claimed in any one of claims 119 to 121 wherein the concentration of water soluble polymer in the liquid medium is 0.3%.

123. A method as claimed in any one of claims 98 to 118 wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to prevent the nematode worms from sticking to the wells of the multi-well plate.

124. A method as claimed in claim 123 wherein the water soluble polymer is polyethylene glycol, polyvinyl alcohol or polyvinylpyrrolidone.

125. A method as claimed in claim 123 or claim 124 wherein the concentration of water soluble polymer in the liquid medium is from 0.01% to 10%.

126. A method as claimed in claim 125 wherein the concentration of water soluble polymer in the liquid medium is 0.1%.

127. A method of identifying chemical substances which have potential pharmacological activity using nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers of hermaphrodite nematode worms into each of the wells of a multi-well assay plate;

(b) dispensing substantially equal numbers of male nematode worms into each of the wells of the said multi-well assay plate;

(c) contacting the nematode worms with a sample of a chemical substance; and

(d) detecting the amount of eggs or offspring produced using non-visual detection means.

128. A method of determining the mode of action of a chemical substance using nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers of hermaphrodite nematode worms into each of the wells of a multi-well assay plate;

(b) dispensing substantially equal numbers of male nematode worms into each of the wells of the said multi-well assay plate wherein the male worms form a panel of different mutant, transgenic or humanized nematode worms;

(c) contacting the nematode worms with the chemical substance; and

(d) detecting the amount of eggs or offspring produced using non-visual detection means.

129. A method of identifying chemical substances which modulate the effect of a first compound, which compound has a defined effect on nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers of hermaphrodite nematode worms into each of the wells of a multi-well assay plate;

(b) dispensing substantially equal numbers of male nematode worms into each of the wells of the said multi-well assay plate;

(c) contacting the nematode worms with the first compound;

(d) contacting the nematode worms with a further chemical substance; and

(e) detecting the amount of eggs or offspring produced using non-visual detection means.

130. A method as claimed in claim 129 wherein the second chemical substance suppresses the defined effect of the first compound on the nematode worms.

131. A method as claimed in claim 129 wherein the second chemical substance enhances the defined effect of the first compound on the nematode worms.

132. A method as claimed in any one of claims 127 to 131 wherein the nematode worms are microscopic nematodes.

133. A method as claimed in claim 132 wherein the nematode worms are *C. elegans* or *C. briggsae*.

134. A method as claimed in claim 133 wherein the hermaphrodite nematode worms and/or the male nematode worms are mutant, transgenic or humanized *C. elegans*.

135. A method as claimed in claim 134 wherein the transgenic *C. elegans* express a transgene comprising a toxic gene.

136. A method as claimed in claim 135 wherein said toxic gene encodes encodes ataxin, alpha-synuclein, ubiquitin, the tau gene product, the Huntington's gene product, the best macular dystrophy gene product, the age-related macular dystrophy product or the unc-53 gene product.

137. A method as claimed in claim 135 or claim 136 wherein expression of the toxic gene is driven by the her-1 P2 promoter, the mab-18 promoter or the spe-T1 promoter.

138. A method of identifying chemical substances which have potential pharmacological activity using nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers of hermaphrodite nematode worms into each of the wells of a multi-well assay plate;

(b) contacting the nematode worms with a sample of the chemical substance; and

(c) detecting the amount of eggs or offspring produced using non-visual detection means.

139. A method of determining the mode of action of a chemical substance using nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers of a panel of different mutant, transgenic or humanized hermaphrodite nematode worms into each of the wells of a multi-well assay plate;

(b) contacting the nematode worms with the chemical substance; and

(c) detecting the amount of eggs or offspring produced using non-visual detection means.

140. A method of identifying further components of the biochemical pathway on which a compound having a defined effect on nematode worms acts, which method comprises the steps of:

(a) subjecting a population of nematode worms to random mutagenesis;

(b) dispensing one mutagenized F1 nematode worm into each of the wells of a multi-well assay plate;

(c) allowing the F1 nematode worm to generate F2 offspring;

(d) contacting the nematode worms with the compound; and

(e) detecting the amount of eggs or offspring produced using non-visual detection means.

141. A method as claimed in claim 140 which further comprises steps of isolating a gene which is mutated in nematode worms which exhibit changes in the amount of eggs or offspring produced in part (e) using genetic techniques.

142. A method of identifying chemical substances which modulate the effect of a first compound, which compound has a defined effect on nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers of hermaphrodite nematode worms into each of the wells of a multi-well assay plate;

(b) contacting the nematode worms with the first compound;

(c) contacting the nematode worms with a further chemical substance; and

(d) detecting the amount of eggs or offspring produced using non-visual detection means.

143. A method as claimed in claim 142 wherein the second chemical substance suppresses the defined effect of the first compound on the nematode worms.

144. A method as claimed in claim 142 wherein the second chemical substance enhances the defined effect of the first compound on the nematode worms.

145. A method as claimed in claim 138 wherein the hermaphrodite nematode worms are mutant, transgenic or humanized *C. elegans*.

146. A method as claimed in claim 145 wherein the transgenic *C. elegans* express a transgene comprising a toxic gene.

147. A method as claimed in claim 146 wherein said toxic gene encodes ataxin, alpha-synuclein, ubiquitin, the tau gene product, the Huntington's gene product, the best macular dystrophy gene product, the age-related macular dystrophy product or the unc-53 gene product.

148. A method as claimed in claim 146 or claim 147 wherein expression of the toxic gene is driven by the lin-31 promoter, the egl-17 promoter, the unc-17 promoter or the unc-53 promoter.

149. A method as claimed in claim 134 or claim 145 wherein the transgenic *C. elegans* express a marker molecule.

150. A method as claimed in claim 149 wherein the marker molecule is an autonomous fluorescent protein.

151. A method as claimed in any one of claims 127 to 150 wherein the step of detecting the amount of eggs or offspring produced comprises adding a specific antibody which binds to eggs, L1 stage, L2 stage, L3 stage or L4 stage nematodes and detecting complexes formed by binding of the antibody to eggs, L1 stage, L2 stage, L3 stage or L4 stage nematodes using non-visual detection means.

152. A method as claimed in any one of claims 127 to 151 wherein the non-visual detection means is a multi-well plate reader.

153. A method as claimed in any one of claims 127 to 150 wherein the step of detecting the amount of eggs or offspring comprises directly counting the numbers of eggs or offspring using a FANS device.

154. A method as claimed in any one of claims 127 to 150 wherein the step of detecting the amount of eggs produced comprises detecting the activity an enzyme released from the eggs on hatching.

155. A method as claimed in claim 154 which comprises detecting the activity of chitinase released from the eggs on hatching.

156. A method as claimed in any one of claims 127 to 155 wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to increase the viscosity of the medium.

157. A method as claimed in claim 156 wherein the water soluble polymer is carboxymethyl cellulose, low melting point agarose or polyethylene glycol.

158. A method as claimed in claim 157 wherein the water soluble polymer is medium viscosity carboxymethyl cellulose.

159. A method as claimed in any one of claims 156 to 158 wherein the concentration of water soluble polymer in the liquid medium is 0.3%.

160. A method as claimed in any one of claims 127 to 155 wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to prevent the nematode worms from sticking to the wells of the multi-well plate.

161. A method as claimed in claim 160 wherein the water soluble polymer is polyethylene glycol, polyvinyl alcohol or polyvinylpyrrolidone.

162. A method as claimed in claim 160 or claim 161 wherein the concentration of water soluble polymer in the liquid medium is from 0.01% to 10%.

163. A method as claimed in claim 162 wherein the concentration of water soluble polymer in the liquid medium is 0.1%.

164. A method of identifying chemical substances which have potential pharmacological activity using nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers of hermaphrodite nematode worms into each of the wells of a multi-well assay plate;

(b) contacting the nematode worms with a sample of the chemical substance; and

(c) detecting changes in the defecation behaviour of the nematode worms using a non-visual detection means.

165. A method of determining the mode of action of a chemical substance using nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers of a panel of different mutant, transgenic or humanized nematode worms into each of the wells of a multi-well assay plate;

(b) contacting the nematode worms with the chemical substance; and

(c) detecting changes in the defecation behaviour of the nematode worms using a non-visual detection means.

166. A method of identifying further components of the biochemical pathway on which a compound having a defined effect on nematode worms acts, which method comprises the steps of:

(a) subjecting a population of nematode worms to random mutagenesis;

(b) dispensing one mutagenized F1 nematode worm into each of the wells of a multi-well assay plate;

(c) allowing the F1 nematode worm to generate F2 offspring;

(d) contacting the nematode worms with the compound; and

(e) detecting changes in the defecation behaviour of the nematode worms using a non-visual detection means.

167. A method as claimed in claim 166 which further comprises steps of isolating a gene which is mutated in nematode worms which exhibit changes in the defecation rate in part (e) using genetic techniques.

168. A method of identifying chemical substances which modulate the effect of a first compound, which compound has a defined effect on nematode worms, which method comprises the steps of:

(a) dispensing substantially equal numbers of nematode worms into each of the wells of a multi-well assay plate;

(b) contacting the nematode worms with the first compound;

(c) contacting the nematode worms with a further chemical substance; and

(d) detecting changes in the defecation behaviour of the nematode worms using a non-visual detection means.

169. A method as claimed in claim 168 wherein the second chemical substance suppresses the defined effect of the first compound on the nematode worms.

170. A method as claimed in claim 168 wherein the second chemical substance enhances the defined effect of the first compound on the nematode worms.

171. A method as claimed in claim 170 wherein the nematode worms are microscopic nematodes.

172. A method as claimed in claim 171 wherein the nematode worms are *C. elegans* or *C. brigssae*.

173. A method as claimed in claim 172 wherein the nematode worms are mutant, transgenic or humanized *C. elegans*.

174. A method as claimed in claim 173 wherein the said mutant *C. elegans* exhibit abnormal defecation behaviour.

175. A method as claimed in claim 174 wherein the mutant *C. elegans* are constipated.

176. A method as claimed in claim 174 wherein said transgenic *C. elegans* express a transgene comprising a toxic gene.

177. A method as claimed in claim 176 wherein said toxic gene encodes encodes ataxin, alpha-synuclein, ubiquitin, the tau gene product, the Huntington's gene product, the best macular dystrophy gene product, the age-related macular dystrophy product or the unc-53 gene product.

178. A method as claimed in claim 176 or claim 177 wherein expression of the toxic gene is driven by the unc-43 promoter or the unc-25 promoter.

179. A method as claimed in any one of claims 164 to 178 wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to increase the viscosity of the medium.

180. A method as claimed in claim 179 wherein the water soluble polymer is carboxymethyl cellulose, low melting point agarose or polyethylene glycol.

181. A method as claimed in claim 180 wherein the water soluble polymer is medium viscosity carboxymethyl cellulose.

182. A method as claimed in any one of claims 179 to 181 wherein the concentration of water soluble polymer in the liquid medium is 0.3%.

183. A method as claimed in any one of claims 164 to 178 wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to prevent the nematode worms from sticking to the wells of the multi-well plate.

184. A method as claimed in claim 183 wherein the water soluble polymer is polyethylene glycol, polyvinyl alcohol or polyvinylpyrrolidone.

185. A method as claimed in claim 183 or claim 184 wherein the concentration of water soluble polymer in the liquid medium is from 0.01% to 10%.

186. A method as claimed in claim 185 wherein the concentration of water soluble polymer in the liquid medium is 0.1%.